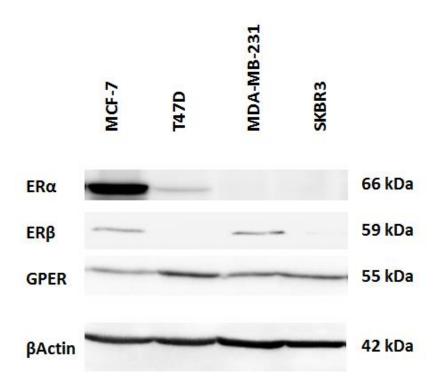
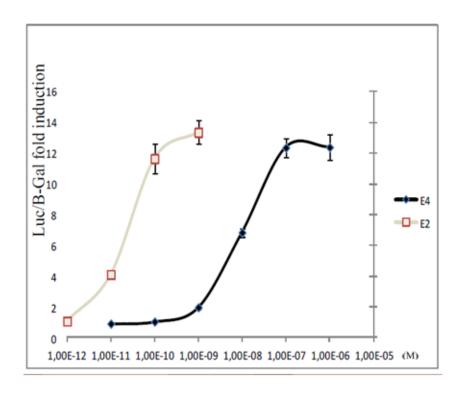
Combined estrogenic and anti-estrogenic properties of estetrol on breast cancer may provide a safe therapeutic window for the treatment of menopausal symptoms

**Supplementary Material** 



Suppl Figure 1

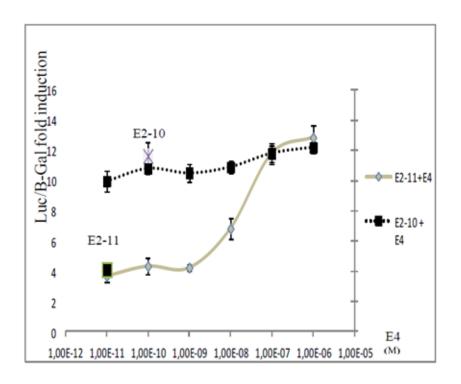
Estrogen receptor status in MCF-7, T47D, MDA-MB-231 and SKBR3 cells.  $ER\alpha$ ,  $ER\beta$  and GPER expression detected by immunoblotting.



## Suppl Figure 2

## Transactivation of an ERE-Luc reporter gene.

MCF-7 cells were transfected with the ERE-Luciferase reporter and treated with increasing concentrations of E2 (grey curve) and E4 (black curve). Results are expressed as mean  $\pm$  SEM fold induction for the Luciferase normalized by  $\beta$ -galactosidase activation.



## Suppl Figure 3

## Transactivation of an ERE-Luc reporter gene: impact of E2+E4.

MCF-7 cells were transfected with the ERE-Luciferase reporter and treated with different combinations of E2+E4. E4 was added at increasing concentrations in the presence of E2 at 2 different concentrations ( $1x10^{-11}M$  or  $1x10^{-10}M$ ). Results are expressed as mean  $\pm$  SEM fold induction for the Luciferase normalized by  $\beta$ -galactosidase activation.